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A definition of flare in low back pain (LBP): A multiphase process involving perspectives of individuals with LBP and expert consensus



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Title: A definition of *flare* in low back pain (LBP): A multiphase process involving perspectives of individuals with LBP and expert consensus.

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- Low back pain (LBP) fluctuates, but not all are considered important by patients
- LBP “Flare” is a meaningful fluctuation but is poorly defined, limiting its utility
- Flare was defined by a multiphase process with consumer input and expert consensus
- LBP flare is defined by concepts of worsening of symptoms plus broader aspects
- Flare involves impact on function and/or emotions

ABSTRACT

Low back pain (LBP) varies over time. Consumers, clinicians and researchers use various terms to describe fluctuations of LBP symptoms. Although “*flare*” is commonly used to describe symptom fluctuation, there is no consensus on how it is defined. This study aimed to obtain consensus for a LBP flare definition using a mixed-method approach. Step 1 involved derivation of a preliminary candidate flare definition based on thematic analysis of consumers’ views in consultation with an expert consumer writer. In Step 2, a workshop was conducted to incorporate perspectives of LBP experts into the preliminary flare definition, which resulted in two alternative LBP flare definitions. Step 3 refined the definition using a two-round Delphi consensus process with experts in musculoskeletal conditions. The definition favoured by experts was further tested with individuals with LBP in Step 4, using the definition in three scenarios. This multiphase study produced a LBP flare definition that distinguishes it from other LBP fluctuations, represents views of consumers, involves expert

consensus, and is understandable by consumers in clinical and research contexts: “*A flare-up is a worsening of your condition that lasts from hours to weeks that is difficult to tolerate and generally impacts your usual activities and/or emotions*”.

Perspective

A multiphase processes produced a low back pain (LBP) flare definition that distinguishes it from other LBP fluctuations, involves expert consensus and represents consumers' views.

Keywords: Low back pain, flare, flare-up, definition, consensus.

INTRODUCTION

Low back pain (LBP) is the most burdensome musculoskeletal condition worldwide [7], affects all ages [17], and contributes to inequality globally [2]. Most individuals experience LBP at least once and for many, LBP is a lifelong problem with trajectories marked by fluctuations [1,14,15,18,28]. Terms such as *acute*, *subacute* and *chronic*, provide little or no information regarding symptom variation, and don't discriminate between *chronic* LBP and multiple *acute* periods. The terms *episodes* [10,12,30], *recurrences* [12,24] and *flares* [23,27,31] are used to describe fluctuations, and may characterize LBP trajectories, but it is unclear how they are defined and differ. *Episodes* and *recurrences* are defined as specific fluctuations preceded by a symptom-free period [12,24,25]. However, not all fluctuations meet this criterion. Although most experience LBP variation (short/long term [14]), not all fluctuations are considered important by individuals [23].

Determination of which variations are important remains an issue. Many with LBP and other musculoskeletal conditions describe “*flare/flare up*” as a distinct type of symptom fluctuation [16,19,21,29]. Flares are not necessarily preceded by a symptom-free period and commonly represent transient worsening [23,27,31]. An important distinction from other fluctuations is that individuals indicate flare involves domains other than pain. A systematic review of flare definitions in musculoskeletal conditions suggested it cannot be reduced to consideration of pain, but is a multifaceted experience marked by features such as impact on function and emotions [9]. Individuals with LBP support this notion [23]. Further, workers consider flares involve activity limitations, participation restrictions, fear of symptom worsening, and need for help to manage symptoms [31]. Flares are a burdensome aspect of LBP [3,8,31]. They disrupt work ability and increase disability and work absenteeism [26,27]. Notably, consideration of flares differs between individuals with LBP and clinicians. Whereas clinicians focus on clinical signs, patients have a broader biopsychosocial view

[9,11]. Flares are likely to be important to outcome in clinical practice and clinical/epidemiological research. Accurate measures/definitions are required, particularly as flare may have different meanings for individuals with pain, clinicians and researchers.

A clear definition of a LBP flare is necessary, yet there is no consensus regarding what it should include. LBP flare was initially described as *'a phase of pain superimposed on a recurrent or chronic course...a period (usually a week or less) when back pain is markedly more severe than is usual...must meet criteria for recurrent or chronic pain, and be able to identify the beginning (and the end if the flare-up has resolved) of a period when back pain was substantially more intense than usually experienced'* [30]. This definition was applied to people with recurrent/chronic LBP, and adapted to acute LBP [26]. The definition's foundation is unclear, and it does not align with the multidimensionality expressed by individuals with LBP.

This study aimed to develop a definition for LBP flare that distinguishes it from other fluctuations. The study involved multiple steps that considered perspectives from experts and individuals with LBP to achieve a definition for research and clinical practice.

METHODS

This mixed methods study to derive a definition of LBP flare comprised four steps: 1) derivation of LBP flare definition from perspectives of individuals with LBP; 2) incorporation of experts' perspectives in a preliminary LBP flare definition at the Low Back and Neck Pain Forum (Buxton UK, June 2016); 3) a Delphi process with experts to refine the definition and reach consensus expert opinion; and 4) qualitative testing of the definition with individuals with LBP. Ethical approval was obtained from the Human Research Ethics Committee of the University of Queensland (2017000183; 2015001094).

Step 1: Derivation of LBP flare definition from qualitative research on consumers' perspectives

A definition of flare was proposed on the basis of findings of qualitative research conducted with 130 individuals who had previous experience with LBP [23]. Five authors (PH, NC, JS, MF, JM) met on 3 occasions to consider consumers' perspective and discuss terminology to reflect the features that distinguish flare from other symptom fluctuations. The initial proposed definition was refined in consultation with an expert consumer writer (TD).

Step 2: Incorporation of experts' perspectives in preliminary LBP flare definition

A workshop was held at the International Forum for Back and Neck Pain Research in Primary Care (Buxton UK, June 2016) with a group of 19 experts in LBP. After a brief introduction to the topic, the candidate flare definition derived from Step 1 was presented. This step aimed to integrate perspectives of experts into the candidate flare definition. The meaning of the definition as a whole, and the specific selection of words were discussed. At the end of the workshop participants were invited to contribute to Step 3. After the workshop, four authors met (PH, NC, JS and MF) to discuss modifications to the definition based on the workshop discussions and notes made during the workshop by PH, MF and NC. Four candidate definitions were developed with slight variation in wording, and then refined to two that reduced the definition to single sentences, and to improve wording based on consultation with consumer writer.

Step 3: Delphi process to refine definition and reach consensus expert opinion

A two-round Delphi process [13] was conducted to: 1) obtain feedback from a diverse group of international experts regarding the two proposed definitions for flare, and 2) re-present a refined definition (based on feedback from round 1) to the participants to evaluate its acceptability. The Delphi process was implemented online via a web-based system

(Google Drive). Sixty-two experts were invited to participate in the Delphi process: 19 participants of the Step 2 workshop, 19 members of the organising committee of the International Forum for Back and Neck Pain Research in Primary Care, and 24 other individuals with expertise in flare in LBP or related conditions, or international reputation in research related to musculoskeletal pain. Contributors were to meet at least 2 of the following criteria; at least 5 papers in previous 3 years related to musculoskeletal pain; invitation to present keynote lecture at international conference related to musculoskeletal pain; or contribution to clinical practice guideline or major systematic review in musculoskeletal pain). The panel included representation from the following professions: physiotherapy (23), rheumatology (6), epidemiology (4), chiropractic (4), primary care (3), medicine (other) (3), orthopaedic surgery (2), psychiatry (1), psychology (1), occupational therapy (1), and medical science (1). A patient advocate was also included in this Delphi process.

Round 1: In Round 1 the two revised versions of the preliminary flare definition (Step 2) were presented to the panel. Round 1 (May 2017) participants were asked to: (1) rate each definition as acceptable or unacceptable; (2) indicate a preferred definition or indicate that neither definition was appropriate; and (3) provide comment on the wording and content of proposed definitions. The percentages of acceptable/unacceptable for each definition, preferred definition, and individuals who considered both definitions to be unacceptable were calculated. It was decided *a priori* that if a definition was preferred by at least 70% of participants (27) and was considered unacceptable by less than 30%, no further Delphi rounds would be required. If these criteria were not met, the lowest ranked definition would be removed and the retained definition would be modified in response to comments from the Delphi contributors. Feedback received from contributors was reviewed and considered by the core study team (PH, NC, JS and MF). This review resulted in several modifications of flare candidate definition 2, which was assessed in Round 2.

Round 2: The revised version of definition 2 was presented to the Delphi Panel (August 2017). Participants who contributed to Round 1 were invited to participate in Round 2 (50 out of 61 potential participants agreed). Round 2 participants were asked to indicate the degree to which they considered the modified definition to be acceptable using a scale from 1 to 10 (1 – strongly disagree, 10 – strongly agree). If they considered that the definition was unacceptable, a justification was requested. Two e-mail reminders were sent to maximise response rate. It was established *a priori* that the definition would be accepted and no further Delphi rounds would be conducted if it received a mean acceptability score of 7 or greater. The mean score was calculated and feedback was considered by the core study group (PH, NC, JS and MF). A minor modification of the definition was made related to duration of flare.

Step 4: Testing understanding of definition with individuals with LBP

Step 4 aimed to determine; i) whether the final LBP flare definition was understandable to individuals with LBP, and ii) whether they would know how to act on this definition in relevant contexts. PH and JS designed three purpose-built scenarios (Table 1) to depict situations where an individual with LBP might be expected to recognise a flare as; (i) a reason to take action in response to a flare (e.g. take medication); (ii) a prompt to contact a researcher in a study of flare to report their symptom status; and (iii) a measure of outcome after a treatment. Participants were provided with the flare definition and one of the three scenarios (random allocation) during an audio-recorded telephone consultation by JS and NC. If participants could determine how to respond appropriately to the scenarios with the embedded flare description, the participant was deemed to have understood the definition. Further confirmation was sought through follow-up questions including requests to: paraphrase the flare definition, clarify whether they had experienced flares of their symptoms according to the definition, and to discuss how they differentiated a flare from other

fluctuations of their symptoms. Analysis was iterative using four stages. Stage 1: JS and NC wrote notes regarding whether the participants they interviewed appeared to understand the scenarios based on their responses to the four questions outlined above. These researchers also made notes of any other relevant responses from participants. Stage 2: notes were considered between the two researchers and any discrepancies discussed. Stage 3: results, including any discrepancies were discussed with a third researcher (who was not involved in the interview process). Stage 4: overall results were shared with the core research team for input.

TABLE 1 Scenarios used in Step 4.

<p><i>Scenario 1</i></p> <p>Imagine you are participating in university research that is investigating low back pain. You meet with the research team. They asked you a number of questions and take some measurements. Before you leave they ask you to contact them again if you have a <i>flare up</i> of your back pain. The researchers say: “A flare-up is a worsening of your condition that lasts from hours to weeks that is difficult to tolerate and generally impacts your usual activities and/or emotions.”</p> <p><i>Question:</i> Would you know when to contact the researchers again?</p>
<p><i>Scenario 2</i></p> <p>Imagine you are at a consultation with your doctor discussing your low back pain. The doctor asks you to take a particular medication when you are experiencing a <i>flare</i>. She says: “A flare-up is a worsening of your condition that lasts from hours to weeks that is difficult to tolerate and generally impacts your usual activities and/or emotions.”</p> <p><i>Question:</i> Would you know when to take the medication?</p>
<p><i>Scenario 3</i></p> <p>Imagine you are thinking about the success of a treatment for your low back pain. More specifically, you were thinking about whether back pain was better as a result of the treatment. Would you feel like you have improved if your low back pain flare-ups have reduced according to the following definition: “A flare-up is a worsening of your condition that lasts from hours to weeks that is difficult to tolerate and generally impacts your usual activities and/or emotions.”?</p> <p><i>Question:</i> Does a reduction of flare according to this definition mean you have improved?</p>

Individuals were invited to participate through advertisements placed on social media, local community and health centres, word of mouth and a contact list of participants from previous studies of LBP. To be considered eligible participants had to meet the following criteria: 1) 18 years of age and above, 2) ability to communicate in English, and 3) self-identification of current or previous LBP. There was no exclusion for LBP duration or other co-existing pain and co-morbidities. Recruitment was ongoing during analysis and final numbers were decided by the principle of saturation (when no new information relevant to the study was being identified) [5]. Prior to the beginning of each consultation, the interviewer read the participant information sheet to each participant. All consultations were commenced after obtaining verbal consent for study participation and recording.

RESULTS

Step 1: Derivation of the LBP flare definition from consumer's perspectives

Published results of a thematic analysis of an on-line survey confirmed that people who experience LBP consider flare to be a type of fluctuation which involves other domains in addition to pain (15). The core research team (PH, NC, JS and MF) discussed how best to encapsulate; (i) the dimensions of flare beyond an increase in pain, (ii) temporal features, and (iii) other domains that would distinguish flare from other fluctuations of symptoms. Emphasis was placed on making the definition simple using terminology that would be understandable to consumers, clinicians and researchers. Consultation with the expert consumer health writer (TD) highlighted that some terms (e.g. 'function') would not be clear to consumers. The proposed definition was: *"A flare is an increase in pain or other related symptoms that lasts from hours to weeks and is difficult to settle. You may also have mood changes and/or difficulty with your normal activity"*.

Step 2: Incorporation of experts' perspectives in the preliminary LBP flare definition

The candidate flare definition was presented to the workshop attendees, who provided feedback in five main areas. Workshop participants' feedback included that:

- i) The phrase "increase in pain and other related symptoms" was considered imprecise. Terminology was simplified to "worsening of symptoms" with the intention to cover all potential symptoms associated with LBP rather than highlighting pain.
- ii) The term "symptoms" was considered too broad and specific symptoms should be listed (e.g. area of symptoms, fatigue, etc). No change was made as such a list would make the definition too long for easy comprehension and would not cover all possible symptoms.
- iii) There was consensus that the definition should be clearer about consequences such as impact/changes in life. Statements such as "difficult to deal with", "has an impact on your function and emotions" and "it is difficult to settle and may be difficult to cope with" were considered.
- iv) The phrase "difficult to settle" was considered unclear. The alternative, "resolve", was also considered inappropriate as it implies complete recovery. Based on this, "difficult to settle" was removed from two versions of the definition but kept in the other two in order to be further discussed.

PH, NC, JS and MF discussed feedback and rephrased the definition in 4 options, which were then refined to two candidate flare definitions with improved word clarity and readability (Table 2). The two candidate definitions were assessed in Step 3.

TABLE 2. LBP flare definition proposed at each step:

Step	Progression of the definition
Step 1: Derivation of LBP flare definition from patient's perspectives	A flare is an increase in pain or other related symptoms that lasts from hours to weeks and is difficult to settle. You may also have mood changes and/or difficulty with your normal activity.
Step 2: Incorporation of experts' perspectives in	Initial proposal: 1) A flare is a worsening of your condition that lasts from hours to

preliminary LBP flare definition	<p>weeks and is difficult to deal with.</p> <p>2) A flare is a worsening of your condition that lasts from hours to weeks and has an impact on your function and emotions.</p> <p>3) A flare is a worsening of your condition that lasts from hours to weeks. It is difficult to settle and has an impact on your function and emotions.</p> <p>4) A flare is a worsening of your condition that lasts from hours to weeks. It is difficult to settle and may be difficult to cope with.</p> <p>Refined to reduce to a single sentence and refine wording based on consultation with consumer writer:</p> <p>1) A flare-up is a worsening of your condition that lasts from hours to weeks that is difficult to improve and hard to cope with.</p> <p>2) A flare-up is a worsening of your condition that lasts from hours to weeks that does not improve easily and may impact your usual activities and emotions.</p>
Step 3: Delphi process to refine definition and reach consensus expert opinion	<p>Round 1:</p> <p>1) A flare-up is a worsening of your condition that lasts from hours to weeks that is difficult to improve and hard to cope with.</p> <p>2) A flare-up is a worsening of your condition that lasts from hours to weeks that does not improve easily and may impact your usual activities and emotions.</p> <p>Round 2:</p> <p>A flare-up is a worsening of your condition that lasts from hours to weeks that is difficult to tolerate and generally impacts your usual activity and/or emotions.</p>
Step 4: Testing understanding of definition with individuals with LBP	No change from Step 3

LBP = low back pain

Step 3: Delphi process to refine definition and reach a consensus expert opinion

Round 1: Fifty of 61 (82%) invited experts agreed to participate. Twelve (24%) preferred Definition 1 (*"A flare-up is a worsening of your condition that lasts from hours to weeks that is difficult to improve and hard to cope with"*), 31 (62%) favoured Definition 2 (*"A flare-up is a worsening of your condition that lasts from hours to weeks that does not improve easily and may impact your usual activities and emotions"*) and seven (14%) did not accept either of the candidate flare definitions. Twenty-three participating experts (46%) considered Definition 1 was unacceptable. Only eleven (22%) experts found Definition 2 unacceptable. As less than 70% participants favoured Definition 2 (62%) and 78% found it acceptable, Definition 1 was rejected. The rationale provided by participants for their choices were

collated and the following issues were identified: i) use of “may” is redundant, ii) minimal symptom intensity and length should be specified, iii) “difficult to improve” is too narrow, iv) “impact on activities and emotions” may not apply to all individuals all of the time. After considering feedback the core research group undertook the following modifications, the word “may” was removed, a minimal length of “a day” was added, “difficult to improve” was replaced by “difficult to tolerate” and the word “generally” was added in order to emphasize that impact on activities and emotions is not always present (Table 2). No changes were made regarding minimal symptom intensity as this directly contrasted the outcome of Step 1 [23]. The modified version of Definition 2 was submitted to a second Delphi round.

Round 2: Of the 50 experts who participated in Round 1, 44 (88%) contributed to Round 2. The average rating of acceptability for the proposed definition was 8.1/10 and 31 participants (89%) provided a rating greater than the *a priori* established cut-off to accept the definition of 7/10. Several participants from Round 2 highlighted that flares can last for hours. As this also concurred with some views from Step 1 [23], “a day” was replaced by “hours”. The final proposed definition for LBP flare is presented in Table 2.

Step 4: Testing understanding of the definition with individuals with LBP

Sixteen consumers participated in the telephone consultations. Most lived in Australia (15); one participant lived in United States of America. Mean age was 43.5 years old (range - 21 to 72). Over half of participants were male (9), had first experienced LBP an average of 16 years (range 1-55) ago, and 69% reported current symptoms.

All participants were able to understand the LBP flare definition as indicated by their response to the scenario they were given. Fifteen of the 16 participants (94%) stated that they would know how to act in the given scenario, for example: “*what you are looking for is the difference between normal and when it gets worse, so yes*” (P10). Another participant said

that he would know how to act based on the definition provided as *"the flare-ups are quite debilitating where I can't stand all the way up and any sort of movement or walking activity can be quite painful. It's quite a specific feeling"* (P11).

Further evidence that our definition of flare was acceptable and understandable to the participants was the fact that all were able to paraphrase the definition, although the level of detail varied between participants. Most participants (87.5%) included most of the definition domains – suggesting that they understood the aspects of the definition that extended beyond simply pain. For instance, P10 *"It's bad enough that interferes with your life and emotions. When you go and 'I can't do that because my back is sore'."* and P1 said that a flare would be *"A worsening of the pain that lasts between hours and weeks – so longer than just a transitory thing – that is bad enough that is interfering with living your life or emotions"*. Only two (12.5%) participants rephrased focusing only on one or two aspects highlighted on the definition provided: one stated that *"A flare is when it becomes worse"* (P3) and the other considered flare as *"The severity of my back pain affecting my day-to-day activities"* (P6). This finding aligned with our expectation that not all people who have LBP flares will experience all aspects included within the definition but that it will be broad enough for most people to relate to.

Almost all participants (15/16) reported previous LBP flares and could relate these flare experiences to the definition provided. Consistent with our definition, when asked about how they would distinguish flares from other fluctuations most highlighted other dimensions in addition to pain. Some participants related flares to the necessity to rest: *"Yeah is when it gets to that level where I just feel really strong pain and I have to actually lay down to feel a bit better, that's when I know I have a flare-up"* (P4). Others stated that flares were intolerable and with broader impact than other fluctuations: *"So when it starts to become intolerable I would say...when it's going to impact my daily life, when it's going to impede on"*

my tasks..." (P15). Another participant highlighted that flares usually go beyond a certain level of variation: "Yeah I think that, in my head anyway, there is a difference between normal, like you know is a bit sore today, to - this is really bothering me! That's the thing you know, it's out of the normal range".

DISCUSSION

This study produced a definition of flare in LBP that is based on the perspectives of individuals with LBP, represents a consensus opinion of experts, and is understandable to individuals with LBP in a range of relevant contexts. The final agreed definition is: *"A flare-up is a worsening of your condition that lasts from hours to weeks that is difficult to tolerate and generally impacts your usual activities and/or emotions"*.

Contextualizing findings

The new proposed definition of LBP flare differs from the definition proposed by Von Korff (see introduction) [30] in several important aspects. First, Von Korff's flare definition only applied to chronic or recurrent LBP. This contrasts the intention of the proposed definition to apply to LBP irrespective of whether it is acute, chronic, recurrent or resolved. Second, Von Korff focused on pain that lasts for one week or less and does not consider longer duration fluctuations in pain. The proposed definition is better aligned with opinions of individuals with LBP [23] and a contemporary understanding of the course of LBP [6,14,28] and takes into consideration symptoms that last for hours to weeks. Third, pain is the only domain considered in Von Korff's flare definition. Consistent with qualitative research investigating individual's perspectives on LBP flares [23], the new definition considers other domains, such as impact on function and emotions, but does not require all those features to be present simultaneously in order to characterize a flare. Taking into

consideration the multidimensional nature of the symptoms considered in flare, we did not include a minimum threshold of change in pain to be considered a flare. This was based on results of the qualitative work that showed people who experience LBP do not consider a pain to be sufficient to characterise a flare [23].

It is important to consider how the proposed definition differs from other types of fluctuations in LBP. Other frequently discussed types of fluctuation are *episode*, which is defined as “*a period of pain in the lower back lasting for more than 24 hours, preceded and followed by a period of at least one month without low back pain*” [12]; and *recurrence* of an episode, defined as “*A return of LBP lasting at least 24hrs with a pain intensity of >2 on an 11-point NRS (>20mm on a 100mm VAS) following a period of at least 30 days pain-free*” [25]. The main distinction from the proposed flare definition is that *episodes* and *recurrences* are specific types of fluctuation that are preceded by a period with no pain, whereas a flare can be any increase in symptoms either superimposed on ongoing symptoms or a pain free state. As such an episode or recurrence might be considered as a specific type of flare. An important consideration is that many individuals with LBP consider that they continue to have the condition of LBP, even when they are symptom free [31], this is congruent with the proposed definition of flare, but might complicate the interpretation of an episode or recurrence.

Multidimensional flare definitions are also described for other musculoskeletal conditions [9]. For instance, in rheumatoid arthritis (RA), flares have been considered to represent “*a cluster of symptoms of sufficient duration and intensity to require (re)initiation, change, or increase in therapy*” [4]. The OMERACT RA group that developed this definition considered a broader range of symptoms in addition to pain and did not establish a minimal threshold of symptom intensity, similar to the proposed LBP flare definition. The multidimensionality of RA flare has subsequently underpinned development of a tool to

quantify changes in multiple domains. Research in gout and psoriatic arthritis have followed a similar trajectory with current work towards instrument to identify flares based on multiple domains [16,20]. In psoriatic arthritis, flares have been defined as “*an overwhelming collection of physical, psychological and emotional symptoms*” [19], which considers the physical flare experience to be linked to psychological and emotional symptoms. This differs slightly from the proposed LBP flare definition, as the emotional changes are not necessarily present in the latter.

Study strengths

The LBP flare definition developed in this study used a multi-step process which was designed to include both participation of individuals with LBP and expert consensus. No previous community-wide input has been obtained to facilitate understanding of LBP flares. As expected for a Delphi approach, not all expert opinions could be included in the final output, and the final definition was the product of agreement by the majority. Some opinions are not reflected in the final definition. For example, some experts did not consider that worsening of symptoms which lasts only a few hours was sufficient to be considered a flare. Some experts' opinions were contrary to the outcome of the qualitative research of individual's perspectives. For instance, some experts did not consider emotional changes as an important feature of LBP flares, whereas this was emphasised by people who experience LBP flares.

Study limitations

Although we made efforts to consider a broad range of experts' perspectives, it is possible that we have excluded valuable opinions of experts who were not invited to participant or did not meet our inclusion criteria for Step 3. Another potential limitation of the current study is that individuals with LBP who participated in Step 4 had first experienced

LBP an average of 16 years (range 1-55) ago. Thus, our sample was biased towards those with long-term recurring or persistent/chronic symptoms. The long-term nature of their LBP would be likely to influence their interpretation and understanding of the LBP flare definition proposed. This may impact the transferability of our findings when considering people who experience flares within a first episode of acute symptoms. The proposed flare definition was tested in hypothetical scenarios rather than in real life contexts. This might not completely reflect external validity. It is important to consider that language and culture might affect the use of the word *flare* and its definition, even among countries where English is the native language. An unanswered question pertaining to the current LBP flare definition and work that has been done for other musculoskeletal conditions is whether a definition alone is sufficient to characterise such fluctuations in LBP or whether tools that quantify change in multiple different domains are required. A comparison of these approaches would be valuable to consider in future research.

Conclusions

This consensus definition takes into account that pain increase alone is unlikely to be sufficient as a definition or marker of a flare in LBP. Our results operationalise a multidimensional flare definition that we have shown is understood by individuals who have experienced LBP if used in clinical and research contexts. The definition is based on the premise that flare measurements (in future LBP studies) should consider a broad community understanding of the term. The new proposed definition considers the importance of understanding disease impact through individuals' perspectives [22] and has taken into account dimensions of LBP considered important by individuals living with LBP, in addition to traditional indicators of clinical state. The multidimensional nature of the definition recognises that not every change in pain is meaningful to people who experience LBP and is aimed to enable differentiation between types of fluctuation across different LBP trajectories

and overcome problems that would likely arise from measurement of treatment efficacy or clinical course based exclusively on pain. This definition will have utility in epidemiologic studies and have clinical implications with respect to measuring treatment efficacy.

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REFERENCES

- [1] Axén I, Leboeuf-Yde C. Trajectories of low back pain. *Best Pract Res Clin Rheumatol* 2013;27(5):601-612.
- [2] Buchbinder R, van Tulder M, Öberg B, Costa LM, Woolf A, Schoene M, Croft P, Buchbinder R, Hartvigsen J, Cherkin D, Foster NE, Maher CG, Underwood M, van Tulder M, Anema JR, Chou R, Cohen SP, Menezes Costa L, Croft P, Ferreira M, Ferreira PH, Fritz JM, Genevay S, Gross DP, Hancock MJ, Hoy D, Karppinen J, Koes BW, Kongsted A, Louw Q, Öberg B, Peul WC, Pransky G, Schoene M, Sieper J, Smeets RJ, Turner JA, Woolf A. Low back pain: a call for action. *Lancet* 2018;391(10137):2384-2388.
- [3] Bunzli S, Watkins R, Smith A, Schütze R, P. OS. Lives on hold: a qualitative synthesis exploring the experience of chronic low-back pain. *Clin J Pain* 2013;29(10):907-916.
- [4] Bykerk VP, Bingham CO, Choy EH, Lin D, Alten R, Christensen R, Furst DE, Hewlett S, Leong A, March L, Woodworth T, Boire G, Haraoui B, Hitchon C, Jamal S, Keystone EC, Pope J, Tin D, Thorne JC, Bartlett SJ. Identifying flares in rheumatoid arthritis: reliability and construct validation of the OMERACT RA Flare Core Domain Set. *RMD Open* 2016;2(1).
- [5] Caelli K, Ray L, Mill J. 'Clear as Mud': Toward Greater Clarity in Generic Qualitative Research. *Int J Qual Methods* 2003;2(2):1-13.
- [6] Chen Y, Campbell P, Strauss VY, Foster NE, Jordan KP, Dunn KM. Trajectories and predictors of the long-term course of low back pain: cohort study with 5-year follow-up. *Pain* 2018;159(2):252-260.
- [7] Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2015;386(9995):743-800.

- [8] Coole C, Drummond A, Watson PJ, Radford K. What concerns workers with low back pain? Findings of a qualitative study of patients referred for rehabilitation. *J Occup Rehabil* 2010;20(4):472-480.
- [9] Costa N, Ferreira ML, Cross M, Makovey J, Hodges PW. How is symptom flare defined in musculoskeletal conditions: A systematic review. *Semin Arthritis Rheum*. 2018. pii: S0049-0172(17)30570-X. doi: 10.1016/j.semarthrit.2018.01.012.
- [10] Croft PR, Macfarlane GJ, Papageorgiou AC, Thomas E, Silman AJ. Outcome of low back pain in general practice: a prospective study. *BMJ* 1998;316(7141):1356.
- [11] Cross M, Dubouis L, Mangin M, Hunter DJ, March L, Hawker G, Guillemin F. Defining Flare in Osteoarthritis of the Hip and Knee: A Systematic Literature Review — OMERACT Virtual Special Interest Group. *J Rheumatol* 2017;44(12):1920-1927.
- [12] de Vet HCW, Heymans MW, Dunn KM, Pope DP, van der Beek AJ, Macfarlane GJ, Bouter LM, Croft PR. Episodes of low back pain: a proposal for uniform definitions to be used in research. *Spine* 2002;27(21):2409-2416.
- [13] Diamond IR, Grant RC, Feldman BM, Pencharz PB, Ling SC, Moore AM, Wales PW. Defining consensus: A systematic review recommends methodologic criteria for reporting of Delphi studies. *J Clin Epidemiol* 2014;67(4):401-409.
- [14] Dunn KM, Campbell P, Jordan KP. Long-term trajectories of back pain: cohort study with 7-year follow-up. *BMJ Open* 2013;3(12).
- [15] Dunn KM, Hestbaek L, Cassidy JD. Low back pain across the life course. *Best Pract Res Clin Rheumatol* 2013;27(5):591-600.
- [16] Gaffo AL, Schumacher HR, Saag KG, Taylor WJ, Dinnella J, Outman R, Chen L, Dalbeth N, Sivera F, Vázquez-Mellado J, Chou CT, Zeng X, Perez-Ruiz F, Kowalski SC, Goldenstein-Schainberg C, Chan L, Bardin T, Singh JA. Developing a provisional definition of flare in patients with established gout. *Arthritis Rheum* 2012;64(5):1508-1517.

- [17] Hartvigsen J, Hancock MJ, Kongsted A, Louw Q, Ferreira ML, Genevay S, Hoy D, Karppinen J, Pransky G, Sieper J, Smeets RJ, Underwood M, Buchbinder R, Hartvigsen J, Cherkin D, Foster NE, Maher CG, Underwood M, van Tulder M, Anema JR, Chou R, Cohen SP, Menezes Costa L, Croft P, Ferreira M, Ferreira PH, Fritz JM, Genevay S, Gross DP, Hancock MJ, Hoy D, Karppinen J, Koes BW, Kongsted A, Louw Q, Öberg B, Peul WC, Pransky G, Schoene M, Sieper J, Smeets RJ, Turner JA, Woolf A. What low back pain is and why we need to pay attention. *Lancet* 2018;391(10137):2356-2367.
- [18] Kongsted A, Kent P, Axen I, Downie AS, Dunn KM. What have we learned from ten years of trajectory research in low back pain? *BMC Musculoskelet Disord* 2016;17(1):220.
- [19] Moverley AR, Vinall-Collier KA, Helliwell PS. It's not just the joints, it's the whole thing: Qualitative analysis of patients' experience of flare in psoriatic arthritis. *Rheumatology* 2015;54(8):1448-1453.
- [20] Moverley AR, Waxman R, de Wit M, Parkinson A, Campbell W, Brooke M, Gossec L, Helliwell PS. Development of a Flare Instrument for Use in Psoriatic Disease: A Report from the 2015 GRAPPA Annual Meeting. *J Rheumatol* 2016;43(5):974-978.
- [21] Murphy SL, Lyden AK, Kratz AL, Fritz H, Williams DA, Clauw DJ, Gammaitoni AR, Phillips K. Characterizing Pain Flares From the Perspective of Individuals With Symptomatic Knee Osteoarthritis. *Arthritis Care Res* 2015;67(8):1103-1111.
- [22] Nelson EC, Eftimovska E, Lind C, Hager A, Wasson JH, Lindblad S. Patient reported outcome measures in practice. *BMJ* 2015;350.
- [23] Setchell J, Costa N, Ferreira M, Makovey J, Nielsen M, Hodges Paul W. What constitutes back pain flare? A cross sectional survey of individuals with low back pain. *Scand J Pain*, Vol. 17, 2017. p. 294.
- [24] Stanton TR, Latimer J, Maher CG, Hancock M. Definitions of recurrence of an episode of low back pain: a systematic review. *Spine* 2009;34(9):E316-E322.

- [25] Stanton TR, Latimer J, Maher CG, Hancock MJ. A modified Delphi approach to standardize low back pain recurrence terminology. *Eur Spine J* 2011;20(5):744-752.
- [26] Suri P, Rainville J, Fitzmaurice GM, Katz JN, Jamison RN, Martha J, Hartigan C, Limke J, Jouve C, Hunter DJ. Acute low back pain is marked by variability: An internet-based pilot study. *BMC Musculoskelet Disord* 2011;12:220-220.
- [27] Suri P, Saunders KW, Von Korff M. Prevalence and characteristics of flare-ups of chronic nonspecific back pain in primary care: a telephone survey. *Clin J Pain* 2012;28(7):573-580.
- [28] Tamcan O, Mannion AF, Eisenring C, Horisberger B, Elfering A, Müller U. The course of chronic and recurrent low back pain in the general population. *Pain* 2010;150(3):451-457.
- [29] Vincent A, Whipple MO, Rhudy LM. Fibromyalgia Flares: A Qualitative Analysis. *Pain Med* 2016;17:463-8.
- [30] Von Korff M. Studying the natural history of back pain. *Spine* 1994;19(18 Suppl):2041S-2046S.
- [31] Young AE, Wasiak R, Phillips L, Gross DP. Workers' perspectives on low back pain recurrence: "it comes and goes and comes and goes, but it's always there". *Pain* 2011;152(1):204-211.